DECISION MEMORANDUM

TO: Administrative File: CAG-00090A
Positron Emission Tomography (PET) Scanner Technology

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SUBJECT: Gamma Camera Imaging

DATE: June 29, 2001

This memorandum serves four purposes: (1) provides a brief description of the recent events at the Centers for Medicare and Medicaid Services (CMS) formerly the Health Care Financing Administration (HCFA), leading to this internally-generated request; (2) describes PET imaging, including both its history, as well as an overview of PET imaging and gamma camera technology; (3) analyzes relevant scientific and clinical literature regarding the differences between full-ring PET and gamma camera imaging; and, (4) delineates the reasoning for the decision on systems appropriate for use with all covered PET indications.

Background

While constructing the decision memorandum for the new indications of FDG-PET reimbursement, a new issue emerged. Which coincidence devices are adequate to provide medically beneficial care to Medicare patients? This core question has evolved into a comparison of gamma cameras versus full- and partial-ring PET imaging systems.

The key considerations in applying this coverage policy to various PET systems include:

1. Virtually all literature that was provided to CMS for review of oncologic indications was conducted using full-ring PET scanners, primarily with

bismuth germanate (BGO) crystals.

2. Multiple documents and a myriad of specialists report "superior performance" with full-ring PET over gamma cameras.

3. CMS based its decision on studies that used a full-ring system, and the conclusions about the medical benefit for specific oncologic indications were, therefore, premised upon the technical performance of these systems.

The decision memorandum issued on December 15, 2000 (CAG-00065) announced Medicare coverage for several new oncologic indications and one new use in the evaluation of myocardial viability. At that time, CMS considered limiting the new coverage to only full-ring PET systems. However, based upon information provided by nuclear medicine experts, CMS believed the assertion that the newer camera-based systems produced images with quality similar to older full-ring systems. The decision was therefore made to include for coverage those camera-based systems with at least a 1-inch thick crystal:

> Coverage is limited to selected high performance PET scanners only. The majority of the evidence submitted to HCFA and available in the scientific literature regarding the diagnostic performance of PET was derived from use of dedicated full-ring bismuth germanate (BGO) PET scanners. As noted above in the last portion of the review of scientific evidence, available studies suggest that some other types of scanners may not perform as well as the full-ring scanners, and may miss clinically important malignant lesions. Coverage for FDG-PET is limited to use of dedicated full-ring PET scanners utilizing BGO, sodium iodide (NaI), or new crystal detector technologies that are equal or superior in performance. Also covered will be partial-ring systems using BGO, partial-ring NaI scanners with at least a 1" thick crystal, and scanners with new crystal detector technologies that are equal or superior in performance. Medicare will not cover any other scanning systems for performing PET, including gamma cameras modified for either non-coincidence or coincidence imaging. For those indications previously covered, PET scanners approved or cleared for marketing by the FDA remain covered.
>
> HCFA is also aware that technology in this area is changing rapidly, and we are anxious to review any available data comparing the image quality, resolution, and sensitivity of newer PET scanners to the data that currently exists relating to the high-performance full-ring PET scanners. A new coverage request containing comparative performance data will be required for HCFA to cover PET studies performed with scanners not listed in this paragraph.

No specific data was provided to CMS to support this design specification.

Immediately following release of CAG-00065, industry representatives raised questions about the empirical basis for the 1-inch crystal size minimum standard. In particular, it was asserted that recent improvements in PET technology resulted in the performance of several camera-based systems that are at least "as good as" the full-ring systems from which the data was obtained to support the new coverage. It was further asserted that some of these high-performance camera-based systems would not meet the design standard promulgated by CMS on December 15, 2000.

CMS recognized that the issue of comparative system performance was both important and complex, and therefore, on January 10, 2001, it opened a new pending coverage decision to specifically investigate camera-based PET scanners and how their performance compares to full-ring PET. In the web posting, CMS requested specific information that might allow the comparison of the clinical performance of different PET systems, i.e., camera-based systems and full-ring PET. In addition to comparative studies, we also requested information on the census of equipment currently in use and the types of machines now being used for PET imaging. Lastly, we requested the industry to describe their criteria for comparing technical performance, image quality, lesion detectability, clinical utility, and outcomes achieved using various systems.

While reviewing the available data on comparison of imaging systems, it became apparent that this issue is far more complex than simply comparing gamma cameras to full-ring systems. There are various generations of machines within each type, different scintillators with obviously different characteristics, and crystals of various thicknesses in the currently used machines. It remains unclear whether all systems give the same diagnostic information or can provide equivalent information with the same acquisition times. Unnecessarily long acquisition times may lead to non-diagnostic studies as patients may not be able to maintain proper positioning. In our April 10, 2001 national coverage decision (coverage instructions released on that date), we noted that: "In the decision memorandum of December 15, 2000, HCFA had indicated that gamma camera systems with at least a 1-inch crystal would be eligible for coverage. However, coverage of PET using camera-based systems is now under further review as a separate national coverage determination. A final decision on what systems other than dedicated PET will be eligible for coverage, if any, will be announced prior to July 1, 2001."

Overview of Technology

Positron-emitting radioisotopes were first discovered in the 1930's. FDG-PET has been evaluated for several decades in pre-clinical models, and is premised upon basic research in biochemistry and biology. This research established the basis of glucose metabolism in normal cell function, as well as its alteration in diseases like cancer, ischemic heart disease, and some neurological disorders. PET imaging relies upon the detection of gamma rays (photons) produced by the decay of radioactive isotopes. Detection of the photons can be performed with stationary single or double-headed gamma cameras, or through rotation of a photon detector around the patient as in single photon emission computed tomography (SPECT).

The first PET scanners were developed in the United States in the 1970's, with the first human scan reported in 1978. Through the early 1980's, PET scans were used primarily in research and predominantly focused on the neurosciences, as scanners were typically only large enough for head studies. Due largely to the emergence of two major commercial suppliers in the mid-1980's, PET scanners are now capable of whole body imaging and increased computer processing capability. Improvements in the technology have had a significant impact on the quality of PET's image reconstruction and display.

PET is a noninvasive diagnostic imaging procedure that assesses the level of metabolic activity and perfusion in various organ systems of the human body. Images are obtained from positron-emitting radioactive tracer substances (radiopharmaceuticals) that are usually administered intravenously to the patient. Where as computerized tomography (CT) and magnetic resonance imaging (MRI) provide information about anatomic structure, the PET image is generally agreed upon to add information on biochemical or physiologic function.

PET scans employ radionuclides with positrons attached to them. Positrons are subatomic particles that resemble electrons, but carry a positive instead of negative charge. When a positron collides with an electron, the particles are annihilated and transformed into two photons. Because they travel in opposite directions, the source of each pair of photons can be identified with great precision. A computer processes the information acquired by the PET scanner and produces an image. In preparation for a PET scan, a positron-labeled compound is administered. The positrons in these compounds are emitted in a matter of minutes requiring image acquisition in a timely fashion.

PET scanners can be broadly defined as full- and partial-ring scanners used exclusively for PET applications and modified gamma cameras used for both PET applications and other nuclear medicine imaging. The technique applied is known as coincidence detection. Scintillation detectors composed of inorganic crystals (sodium iodide 'NaI' and bismuth germanate 'BGO' are the two common types) and photomultiplier tubes are placed on opposite sides of the radiation source. When both detectors produce a signal within a similar time interval, a coincident event has been detected. During a scan, millions of coincidence events provide the information about the quantity and spatial location of the radioisotopes in the body.

Full-ring systems employ one or more full-rings of detectors (each ring is a series of scintillators) that surround the patient. This simultaneous acquisition of data from all projections yields a high count rate with minimal decay of isotope. Partial-ring systems decrease the amount of crystal required since the ring does not entirely circle the patient but the partial rings still employ a series of scintillators. To compensate and maintain image quality, the system rotates the detector around the patient to obtain a three dimensional reconstruction of the image. Conversely, gamma cameras with coincidence detection use two or three-large area gamma camera detectors that rotate around the patient to obtain a full set of angular projections. This design limits the number of simultaneously detected events. Since all these projections are not collected simultaneously the count rates are lower, acquisition time is longer, and decay of isotope must be corrected for. Given the division of PET systems into two groups based on the applied science, this document will proceed to compare and contrast clinical data from "full- and partial-ring" systems to "camera-based" systems.

Recent advances in PET imaging have included the development of new crystal types such as lutetium oxyortho-silicate (LSO), digital detection, attenuation correction, iterative reconstruction, and a host of computer-driven applications to minimize or correct for scatter and/or randoms. Evaluating the quality of images has been the

standard for system comparison and still plays a major role, but to fairly compare systems, one must also consider other variables such as table and acquisition times, final reconstructed image resolution, lesion detection/discrimination ability, and count rates. Such technological upgrades have, in turn, placed added responsibilities upon nuclear medicine technicians and physicians to upgrade their own technical, interpretative, etc. skill sets.

FDG-PET scanning in oncology has several important features. It is minimally invasive, only requiring an intravenous injection. It differentiates lesions based upon a biochemical process, namely increased glucose metabolism, rather than non-specific anatomical criteria (primarily size and location) provided by computerized axial CT or MRI. Finally, there are mathematical models to quantify metabolic activity and actual three-dimensional radioactive bio-distribution objectively, rather than via visual interpretation.

Food and Drug Administration (FDA) approval of PET systems

PET radiopharmaceuticals have been evaluated and approved by the FDA for use as diagnostic imaging agents. Typically, PET radiopharmaceuticals have a short physical half-life and are manufactured using local cyclotrons or generators. In addition, many of the manufacturers of PET radiopharmaceuticals are located in hospitals and clinics, thus differing from the traditional pharmaceutical and device manufacturers that FDA regulates. In addition, many academic institutions have developed several PET radiopharmaceuticals. FDA has been working with the PET community to develop appropriate criteria and procedures to evaluate PET products for safety and effectiveness. On November 21, 1997, the President signed the Food and Drug Administration Modernization Act (FDAMA) into law. Section 121 of FDAMA requires the FDA to develop procedures under subsections (b) or (j) of section 505 (21 United States Code 355) for the approval of PET radiopharmaceuticals.

The current FDA recommendation for evaluating the diagnostic effectiveness of radiopharmaceuticals for imaging is to conduct studies with an external reference standard of truth such as histopathology. Also, other imaging modalities can be used as active controls, such as MRI and CT.

All FDG-PET oncology studies the FDA reviewed contained biopsy information to derive sensitivity and specificity as measurements of FDG-PET performance in detecting malignancy. Sensitivity and specificity are diagnostic efficacy measures that are not dependent on prevalence of disease in a tested population. For this reason, FDA does not discuss positive and negative predictive values of studies, as these are prevalence-dependent. Sensitivity and specificity, however, do vary depending on the test population (types of cancer, concomitant patient conditions, such as diabetes, which may affect the test, etc.).

Evaluating the prospective performance of a new diagnostic modality is based on the initial classification of abnormality by conventional standards. This process does not

allow the new technology to assess cases that are not detected by conventional methods such as CT or MRI. The literature has many studies of these tests´ sensitivities and specificities using pathology as a standard of truth. Defining the PET study population prospectively based on abnormalities found on CT, MRI, or other modalities such as chest x-rays, precludes performance evaluation of PET in patients who may be false-negatives by conventional testing. While the agreement of FDG-PET results with those of CT or MRI in the reviewed studies is useful information, no attempt has been made by FDA to comment on superiority of test performance. It should also be noted that comparisons between CT or MRI scans and PET imaging may not be appropriate, as these other modalities provide anatomical data usually stated as size and location, as opposed to biochemical, metabolic data provided by PET imaging.

The well-controlled studies of Lowe[1] (1998) and Carr[2] (1998) permit estimates of sensitivity and specificity of F-18 FDG PET performance for assessing malignancy in patients with abnormalities found by another imaging modality, and in patients with an existing diagnosis of malignancy. The reported sensitivity and specificity varied with the cancer type and size, and other clinical parameters. The trial designs and hypotheses tested did not study how FDG might be used prospectively. However, given the long history of use of FDG-PET, and the numbers of studies showing consistent findings, these studies collectively demonstrate the clinical relevance of performing F-18 FDG studies in patients with suspicious abnormalities from other testing modalities or pre-existing diagnoses of cancer. These populations are sufficiently different from other types of populations to not permit generalization of results to other populations. However, more studies would be needed if labeling claims were to contain cancer-specific diagnostic or management claims.

The FDA does not require any primary data from human studies to approve a specific PET system. PET machines are approved based on technical performance information that includes some basic verification of image production using phantom positron emitters. A device is approved with respect to the claim it makes. If a manufacturer claims the device can detect a lesion 15 cm in size, and the device demonstrates this claim using phantom positron emitters, then the device is approved. There are no minimum standards for lesion detectability imposed by the FDA. FDG itself was approved for all oncologic indications based on a literature review that produced two high quality studies of diagnostic performance (as referenced above) in oncology, with many FDA disclaimers as to the generalization of the results to all forms of cancer and in different populations.

Census of Currently "In-Use Equipment"

Information provided by the Medical Information Division's Nuclear Medicine Census Database conducted between 1999 and 2000 identified 240 sites where PET procedures are performed including both full-ring and camera-based systems. Review of these sites

[1] Lowe, et al.
[2] Carr, et al.

revealed approximately 9,650 gamma cameras in use, of which 3,366 have two or more heads with 1,674 installed in 1997 or later. Approximately five percent of these are configured for PET (≈500 units). According to industry experts, about 1,674 gamma cameras are potentially upgradable to perform PET imaging, with between 30 and 50 system upgrades annually. Further, at this time, the 500 gamma camera systems produce approximately 1,000 PET scans per week, while the 200 dedicated installed systems produce about 4,000 per week.

Timeline of Events

January 10, 2001	CMS internally generated a formal coverage request
January 18, 2001	Initial meeting with industry representatives
March 20, 2001	Meeting with National Electrical Manufacturers Association (NEMA) representatives and industry
March 23, 2001	Requested scientific data received by CMS
March 26, 2001	1. Meeting with Steve Atkinson (ADAC/Phillips) to review provided data 2. Conference call with representatives from the American College of Nuclear Physicians (ACNP)
April 2, 2001	Follow-up conference call with representatives from the ACNP
April 24, 2001	Phone call with Siemens regarding partial-ring and full-ring systems
May 3, 2001	1. Meeting with NEMA representatives and industry 2. Additional information received from manufacturers
May 4, 2001	Due date extended until May 18, 2001, in order to analyze additional information.
May 18, 2001	Due date extended until June 1, 2001.
June 1, 2001	Due date extended until June 15, 2001.
June 11, 2001	Due date extended until June 30, 2001.

Summary of Evidence

In collaboration with industry and professional societies, we acquired 14 articles and abstracts that attempt to compare camera PET to full-ring PET. Meeting abstracts, along

with full-length, peer-reviewed articles, were included, given the scarcity of published material on this topic. Additionally, we contacted a group using standardized, full-body phantoms for system comparison studies (data not yet available), and we have participated in multiple meetings and telephone calls with clinical and technical experts from industry, academia, and government. To date, few papers address full-body phantoms, clinical outcomes, or compare management of patients with camera PET versus no PET. Literature on the performance of gamma camera performance, compared to full-ring PET systems, was acquired from three main sources:

1. Material provided by a consortium of PET manufacturers on March 23, 2001.

2. Pertinent references from a major recent review article on PET.[3]

3. Literature search conducted by CMS with the key words "gamma camera" and "PET" along with the following inclusion criterion:

    1. Articles must be published in English;
    2. Study must have been performed on human subjects; and
    3. Articles and abstracts must have been completed within the last five years.

In reviewing the literature, we framed the following questions:

1. Is there enough evidence present to make a "reasonable and necessary" determination on gamma cameras versus full-ring PET systems for broad oncology coverage?

2. Does final image detection vary with the use of gamma cameras versus full-ring PET (accepting variation in performance from the various model designs and generations of machines)? If so, are there obvious distinctions in terms of size, location, or cancer types, delineating safe parameters for use?

3. Does the "surrogate" difference in lesion detection translate to substantial changes in patient management and /or outcomes?

4. Can we safely state that "camera PET" is better than conventional imaging alone in the management of oncology indications?" Does camera PET substantially, and positively, impact patient outcomes for the currently covered PET indications?

Table 1 illustrates a system-specific breakdown of studies that compare gamma cameras and full-ring systems. In most instances, full-ring PET is the gold standard for comparison, which raises a strong methodological concern, since only an independent gold standard is robust. Full-ring PET, relative to a reference truth standard such as histopathological findings, will still have both false positive and false negative results, meaning that the use of full-ring PET as a gold standard in itself can generate distorted

[3] Gould, et al.

results. Thus, true sensitivity and specificity of gamma cameras cannot be determined by this method which tends to falsely inflate both of these performance parameters.

Questions 1, 2, and 3 address the evidence overall and specific outcomes information. There does not appear to be enough quality in the existing studies to support unrestricted coverage of all FDA-approved machines. Most studies use a 5/8-inch gamma camera for comparison, with only one study each using a ¾-inch and ½-inch camera. No studies compare full-ring PET to either partial-ring PET or 1-inch camera systems. Gamma cameras, when grouped according to organ systems, have sensitivity shortfalls ranging from 0-36%,[4] [5] [6] [7] [8] [9] [10] [11] [12] [13] relative to full-ring PET, and the even larger discrepancies (abdominal and musculoskeletal) seen in the 1998 Shreve[14] study reportedly reflect a predominance of small lesions. There is considerable variation both within and among different organ system groups.

These papers and expert opinions from industry and NEMA agree that the average camera acquisition is 40-50% longer than full-ring PET for full-body images. The full-ring systems average 30-45 minutes, while average full-body scans on a camera- based system average 60-90 minutes. Further, it should be noted that this margin is narrowing rapidly with significantly shorter scan times, i.e., full-ring PET is 20% shorter than camera PET for that data referenced in recent studies (see Table 1).

Three studies address variations in patient management based on imaging with the different modalities. Approximately 10% of patients were managed differently between the camera and full-ring groups. Lastly, many studies discuss the threshold for 100% size detection between the two systems. Clearly, the larger the lesion the better the correlation between system types. Table 1 presents two studies with a 2.0 cm 100% detection threshold,[15] [16]one study with a 1.8 cm 100% detection threshold,[17] and two studies with a 100% detection threshold.[18] [19]The challenge is in knowing where this detectability "step-off" becomes clinically significant.

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[4] Boren, et al.
[5] Landoni, et al.
[6] Zimny, et al. (1999)(Eur J Nucl Med)
[7] Zimny, et al. (1999)(Nucl Med)
[8] Tatsumi, et al. (1999)
[9] Delbeke, et al.
[10] Dresel, et al.
[11] Segall, et al.
[12] Berger, et al.
[13] Tatsumi, et al. (2000)
[14] Shreve, et al.
[15] Landoni, et al.
[16] Zimny, et al. (1999)(Eur J Nucl Med)
[17] Zimny, et al. (1999)(Nucl Med)
[18] Berger, et al.
[19] Tatsumi, et al. (2000)

Question 4 specifically addresses the role of camera systems versus conventional imaging alone. An abstract by Dresel[20] from the 46th Annual Meeting of the Society of Nuclear Medicine (SNM) (See Table 1 for additional details) noted that 2 out of 16 patients with recurrent lesions of the mouth or tongue were detected by gamma camera imaging, whereas CT only found a lesion in one of these patients. Similarly, gamma camera imaging diagnosed lymph node involvement in 7 of the 16 patients, compared to 6 out of the 16 with CT. Furthermore, two patients presented with bilateral lymph node involvement via gamma camera PET, whereas in one patient, CT diagnosed only one side correctly. However, primary lesions of the mouth or tongue were detected in 15 of the 16 patients by both gamma camera PET and CT. This very small data set is merely suggestive that gamma camera imaging can outperform CT, particularly since the full study design is not available in this "abstract-only" presentation.

In contrast, an abstract by Tatsumi[21] (47th Annual Meeting of the SNM) reported the following on a series of 30 patients undergoing staging for non-Hodgkin's lymphoma: 159/206 sites (77%) detected by gamma camera PET vs. 164 of 206 sites (80%) by conventional imaging (CT and gallium scanning). This particular data set suggests equivalence between such technologies, subject, of course, to the methodological limitations described above.

CMS Analysis

The main limitation of the available published information on camera-based PET systems is that the data does not provide reliable information about how likely these systems are to identify malignant lesions. The documented sensitivity and specificity primarily determine the reliability of the diagnostic information provided by a PET scan, and therefore, the medical benefit those scans may provide. The main differences in the systems still revolve around lesion detection and the reliability of non-detection, particularly for lesions that are small-to-medium in size. In the practice of oncology, major therapeutic decisions are made based on the presence or absence of small malignant lesions. In fact, the potential value of PET as an added diagnostic modality is its proposed ability to determine whether anatomic abnormalities are malignant. It is the inadequate lesion detection capability for smaller lesions that may critically impact treatment decisions and lead to the potential (inadvertent) harming of patients. All the data used to gain approval was based on studies using full-ring systems. The clinical impact of lower quality images was not considered in any detail at that time.

The clinical utility of camera-based PET is difficult to evaluate if we do not have accurate information on the false positive and false negative rates for these systems when used for the different, covered, oncologic indications. CMS's most recent decision memorandum to cover FDG-PET for use in oncology was based on a careful assessment of the sensitivity and specificity of PET and its ability to detect lesions in real patients with specific clinical settings. This evaluation carefully considered whether PET

[20] Dresel, et al.
[21] Tatsumi, et al. (2000)

provided information additional to what was already provided by CT, MRI and other conventional imaging studies.

Available literature and other information related to comparative performance of different PET systems are quite limited. FDA approval of a PET system documents only that an approved system is safe and successfully produces an image that meets a minimum resolution threshold based on use of phantom positron emitters. FDA approval does not guarantee a standard of clinical performance that is linked to clinical-decision making or patient outcomes, and does not provide an adequate basis to determine that use of PET is medically beneficial for patients with specific malignancies.

There are no clear, comparative, broad indication studies, and only very small, indication-specific studies to compare camera-based PET to full-ring PET. Further, these studies are designed to focus mainly on the intrinsic performance of the scanners, not the evaluation of reconstruction and processing algorithms on the sensitivity and specificity of different systems under conditions of actual clinical use. In other words, after an exhaustive search for empirical data, there is no body of evidence that attests to the medical benefit associated with use of camera-based PET that is comparable to the literature used to arrive at the December 15, 2000 decision memorandum for full-ring PET. The extension of that decision memorandum to camera-based systems, while anecdotally supported by nuclear medicine experts, cannot be clearly justified based on existing clinical and scientific data.

In fact, review of the existing literature on camera-based PET leads to the conclusion, present in several articles, that these systems miss a significant number of small and medium-sized malignant lesions. Because of the limited size of the studies and other methodologic weaknesses, it is not possible to make confident estimates of the frequency with which these different systems produce false positive or false negative results. Furthermore, it is not possible to determine the clinical significance of diagnostic errors that might result from use of these PET technologies. However, given the intended diagnostic role for oncologic uses of PET, it is likely that inaccurate results provided by these imaging systems could lead to errors in treatment, such as early termination of chemotherapy or unnecessary surgical intervention. Without better studies that provide more confident estimates of the sensitivity and specificity from camera-based PET systems, it may not be possible for clinicians to properly interpret the findings from these imaging studies. As predicted by one PET expert in 1998, “the technology will come under criticism because of the mistakes that will be made.” While that comment referred to PET technology several years ago, the current literature reviewed does not refute that conclusion.

Given knowledge now available to CMS, it is likely that the system specifications in the December 15, 2000 decision memorandum were made with insufficient technical information. Based on the coverage request that prompted that decision, and the available data in the scientific literature, it would have been most consistent with existing data to provide coverage only for full- and partial ring systems. By attempting to provide somewhat broader coverage, it was necessary for CMS to extrapolate beyond data

available to us at that time. It is likely that the 1-inch crystal thickness threshold is not a meaningful basis for distinguishing between PET systems. It was asserted to CMS that new, camera-based systems could outperform the full-ring systems for which data was provided to CMS. However, no studies have been provided to CMS since that time that demonstrate either equal or superior clinical performance of these new systems.

Conclusion

The existing literature shows that camera-based systems miss a non-trivial number of small but potentially clinically significant malignant lesions compared with full-ring PET scanners. In addition, available studies do not clearly show that gamma camera imaging can replace or add to the diagnostic information provided by conventional imaging. The studies have only evaluated a small number of camera-based systems in a limited number of oncologic uses. The clinical implications of the potentially missed lesions have not been systematically evaluated. In order to determine whether these systems offer net medical benefit or might inadvertently cause harm, further studies of the technical and/or clinical performance of these systems will be necessary. CMS has decided to draw conclusions about the clinical utility of partial-ring scanners based on the evidence for full-ring systems, due to the fundamental design similarities for these two types of systems. These design characteristics are significantly different than the major design elements and applied science behind gamma cameras modified to perform PET.

Decision

CMS's December 15, 2000 decision memorandum was based on clinical data collected in patients using the full-ring systems with BGO crystals that were in service in the late 1990's. CMS's conclusion that FDG-PET is a reasonable and necessary service for the indications reviewed in the December 15, 2000 memorandum was therefore based on the imaging performance of full-ring systems compared to conventional imaging.

Our review of all available published studies on gamma camera PET systems demonstrates that these devices perform as well as full-ring PET scanners for moderate and large lesions, but may not detect a significant percentage of smaller lesions (approximately 2 cm or less). In addition, available studies do not clearly show that gamma camera imaging can replace or add to the diagnostic information provided by conventional imaging. Newer gamma camera systems may have improved performance, but no clinical data are available on these most recently released systems. Studies used for FDA approval of gamma cameras were based on images produced by "phantoms" or artificial lesions, and therefore do not allow conclusions to be drawn about the clinical utility of these systems for specific clinical applications.

Given this body of scientific information, gamma camera PET, even those systems with crystals at least 1-inch in thickness, will not be covered for the clinical indications which are newly-covered, based upon the December 15, 2000 decision memorandum.

In addition, for those indications already covered prior to the December 15, 2000 decision memorandum, PET imaging must be performed on either FDA-approved full- or partial-ring scanners, or coincidence systems that have the following features:

- Crystal at least 5/8-inch thick
- Techniques to minimize or correct for scatter and/or randoms
- Digital detectors and iterative reconstruction

Scans performed with gamma camera PET systems with crystals thinner than 5/8-inch will NOT be covered. In addition, scans performed with systems with crystals greater than or equal to 5/8-inch in thickness, which do not meet the other listed design characteristics, are NOT covered.

CMS will formally reconsider these limitations on coverage for gamma cameras after December 31, 2002. Coverage would be provided for gamma cameras 1) if these systems can demonstrate performance equivalent to or better than the full-ring PET systems for which data was submitted in support of the December 15, 2000 decision memorandum; or 2) if their clinical utility is demonstrated by adequate clinical studies showing that the gamma camera provides diagnostic information that adds to or replaces information provided by conventional imaging. In the absence of such evidence, CMS will consider withdrawing all coverage for gamma camera systems.

CMS is aware of the standards for PET performance measurement recently released by NEMA, called the NU 2-2001 standards. These standards may provide a mechanism for comparing the performance of PET systems with different design features. CMS will work with representatives of industry and the academic community over the next 18 months to explore whether these measurement standards could be reliably used to compare the performance of different PET systems.

Table 1. Performance of Gamma Cameras Relative to Full-Ring PET Systems

Anatomic Location	Author/Year	Type of Gold Standard	Crystal Thickness	Acquis. Time	Sensitivity	Specificity	% Patients w/ Incorr. Staging	Data Specified by Size of Lesion	Miscellaneous Notes
Brain									
	Landoni 1999	BGO Full-ring PET	5/8”	N/A	100%	N/A		Yes: 100% concordance if at least 2.0 cm	
	Delbeke 1999	BGO Full-ring PET	3/8”	Similar	73%	N/A		Yes	
Head and Neck									
	Zimny 1999 (Eur J Nuc Med)	BGO Full-ring PET	5/8”	Similar	89%	N/A		Yes: 100% concordance if at least 2.0 cm	Attenuation-corrected values used.
	Zimny 1999 (Nuklearmedizin)	BGO Full-ring PET	5/8”	Similar	82%	N/A	11%*	Yes: 100% concordance if at least 1.8 cm	*Applies to all tumor types in this article.
	Shreve 1998	BGO Full-ring PET	5/8”	Similar	71%	N/A		No	
	Dresel 1999 (Abstract)	BGO Full-ring PET	3/4”	N/A	100%	N/A		No	Mouth and tongue lesions only.
	Segall 1999 (Abstract)	BGO Full-ring PET	1/2”	Similar	92%	N/A		No	Regional acquisition times for full-ring (25 min) and camera systems (30 min), with same pattern for all other studies described as “similar” in Table 1.
	Berger 2000 (Abstract on Thyroid Cancer)	Full-ring PET, Unspecified Crystal	5/8”	N/A	69%	N/A	16%	Yes: 100% concordance if at least 1.5 cm	
Lung									
	Tatsumi 1999	Histopathology	5/8”	N/A	96% (Full-ring PET 100%)	N/A		Yes	Stronger study design with pathologic gold standard.
	Shreve 1998	BGO Full-ring PET	5/8”	Similar	93%	N/A		Yes	

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Anatomic Location	Author/Year	Type of Gold Standard	Crystal Thickness	Acquis. Time	Sensitivity	Specificity	% Patients w/ Incorr. Staging	Data Specified by Size of Lesion	Miscellaneous Notes
Thorax/ Mediastinum									
	Landoni 1999	BGO Full-ring PET	5/8”	N/A	84%	N/A		Yes: 100% concordance if at least 2.0 cm	
	Boren 1999	BGO Full-ring PET	5/8”	Similar	83%	N/A		Yes: 100% concordance if at least 1.5 cm	
	Zimny 1999 (Eur J Nuc Med)	BGO Full-ring PET	5/8”	Similar	84%	N/A		Yes: 100% concordance if at least 2.0 cm	
	Zimny 1999 (Nuklearmedizin	BGO Full-ring PET	5/8”	Similar	64%	N/A	11%	Yes: 100% concordance if at least 1.8 cm	
	Shreve 1998	BGO Full-ring PET	5/8”	Similar	65%	N/A		Yes	
	Tatsumi 1999 • Mediastinal lymph nodes • Hilar lymph nodes	Histopathology	5/8”	N/A	78% (Full-ring PET 78%) 75% (Full-ring PET 100%)	93% (Full-ring PET 79%) 90% (Full-ring PET 84%)		No	Note improved specificity of gamma camera over full-ring PET.
	Segall 1999 (Abstract)	BGO Full-ring PET	1/2”	Similar	88%	N/A		No	

Table 1. Performance of Gamma Cameras Relative to Full-Ring PET Systems

Anatomic Location	Author/Year	Type of Gold Standard	Crystal Thickness	Acquis. Time	Sensitivity	Specificity	% Patients w/ Incorr. Staging	Data Specified by Size of Lesion	Miscellaneous Notes
Abdomen/ Pelvis									
	Boren 1999	BGO Full-ring PET	5/8”	Similar	Hepatic 67% Extrahepatic 78%	N/A		Yes, but concordance data N/A	
	Zimny 1999 (Eur J Nuc Med)	BGO Full-ring PET	5/8”	Similar	87%	N/A		Yes: 100% concordance if at least 2.0 cm	
	Zimny 1999 (Nuklearmedizin	BGO Full-ring PET	5/8”	Similar	93%	N/A	11%	Yes: 100% concordance if at least 1.8 cm	High proportion of lymphomas, with high glucose consumption.
	Shreve 1998	BGO Full-ring PET	5/8”	Similar	23%	N/A		Yes	Note different composition of tumors than Zimny 1999.
	Segall 1999 (Abstract)	BGO Full-ring PET	1/2”	Similar	71%	N/A		No	
Musculo-skeletal									
	Shreve 1998	BGO Full-ring PET	5/8”	Similar	50%	N/A		Yes	
	Segall 1999 (Abstract)	BGO Full-ring PET	1/2”	Similar	92%	N/A		No	
Non-Hodgkin’s Lymphoma	Tatsumi 2000 (Abstract)	Independent Clinical Evaluation	5/8”	N/A	77% (Full-ring PET 87%)	N/A	7%	Yes: 100% concordance if at least 1.5 cm	

Table 1. Performance of Gamma Cameras Relative to Full-Ring PET Systems